Results: Overall 1069 patients enrolled in the study, and 558 had 12-month data available as of September 30, 1999. At baseline the mean level of bothersomeness of the condition was 70.8 on a scale from 0 (not bothersome at all) to 100 (as bothersome as I can imagine). Patients reported a 41.5% improvement over baseline in the bothersomeness of the condition after 3 months, a 45.2% improvement after 9 months, and a 49.7% improvement after 12 mos of treatment ($p<0.0001$ for each comparison with baseline). At baseline 69.6% of patients reported that nighttime awakenings due to UI interfered with daily activities some, most or all the time compared with 31.3% of patients after 3 months of treatment. At baseline 39.5% of patients indicated that at least 5 of 9 daily activities (household chores, relationships, exercise, work, etc.) were impacted by urine loss frequently or all the time; after 3 months of treatment, the percentage decreased to only 13.4% of patients. Adverse effects were the most common cause for discontinuation during the first 3 months and included dry mouth and other anticholinergic effects. Adverse effects were less frequently the cause for discontinuation after 9 months. The total rate of discontinuation over the 12 months due to adverse effects was 22.9%, including 8.1% for dry mouth and 6.3% for other anticholinergic effects.

Reasons for discontinuation:	Prior to 3 mos.	9-12 mos.
Adverse effects (total)	14.2%	1.6%
Dry mouth	4.5%	0.7%
Other anticholinergic	5.0%	0.2%
Lack of efficacy	3.8%	0%

Discontinuation of treatment due to lack of efficacy was low (3.8%) prior to 3 months and did not occur after 9 months. After 3 and 6 months of treatment, 74.7% and 80.3% of patients, respectively, reported the drug worked well, very well or excellent, and 79.2% and 86.8%, respectively, were pleased, very pleased or extremely pleased with treatment.

Conclusions: In this long-term, community-based study, discontinuation of controlled-release oxybutynin treatment due to dry mouth was much lower than that reported in the literature for conventional oxybutynin and occurred mostly in the first 3 months. Treatment of overactive bladder with controlled-release oxybutynin substantially improved the quality of life of patients as assessed by four different instruments.

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DETRUSOR INSTABILITY - ARE GAP JUNCTIONS RESPONSIBLE FOR INCREASED MEMBRANE EXCITABILITY?

Aims of Study: Gap junctions are specialized cell membrane structures, which allow for rapid communication between adjacent cells. They permit the rapid propagation of action potentials between cells. Membrane channels (connexons) of one cell form gap junctions, which are aligned with apposing channels from another cell to form patent water filled passages across two membranes. These connexons are composed of the structural protein connexin. Recent work has identified connexin 43 in the human laboring uterus (1).

Brading and Elbadawi have advanced a myogenic basis for detrusor instability. Smooth muscle cells from the detrusor of patients with detrusor instability are more easily excited by direct electrical stimulation when compared with controls. Elbadawi et al (2) identified the presence of 'alien' junctions in elderly patients with detrusor overactivity. They concluded that these junctions were de-differentiated gap junctions capable of mediating electrical coupling between detrusor smooth muscle cells and formed the basis of detrusor instability. They based their conclusions on electron microscopy findings alone. Cell junctions in more rudimentary forms may be difficult to characterize, increasing the likelihood of misclassification and misinterpretation of function. This problem can be overcome by the additional use of immunohistochemistry to identify the junction types.

The aim of this study was to test the hypothesis that detrusor instability was associated with the presence of gap junctions using an immunoperoxidase technique for the identification of connexin 43. Electron microscopy and vinculin immuniohistochemistry were used to assist in the identification of detrusor smooth muscle junctions and other membrane structures.

Methods: Seven women 32 to 68 years old median 55 years with severe detrusor instability and no stress incontinence and 5 controls aged 41 to 64 (median 50) with genuine stress incontinence and stable bladders and no symptoms of sensory/urgency or urge incontinence were studied. Three bladder biopsies, approximately 2-4cm above the trigone and near the midline were taken from each patient. Specimens were processed for electron microscopy by standard methods. Two investigators blinded to the urodynamic diagnosis analyzed the electron micrographs. Specimens were also processed for immunohistochemistry using an immunoperoxidase technique for

the identification of connexin 26 and 43 at an optimal dilution of 1:1,000 and a hydrogen peroxidase labeled antibody to vinculim (dilution of 1:1,750). Infant mouse heart was used as the connexin control and rate small bowel granulation tissue as the vinculin control.

Results: Immunohistochemistry- No cell membrane staining for connexin 26 or 43 was seen in the bladder biopsies of the 5 cases and 4 controls. Entire cell border staining with labeled antibody to vinculin was present in all cases and controls.
Electron Microscopy- No gap junction was identified in any of the cases or controls. Adherens (intermediate)junctions in classic and rudimentary forms were present in all cases and controls. Dense plaques ('hemijunctions') were present on the membranes of all patients and usually a 'complementary' dense plaque could be identified on an adjacent cell membrane. Adherens junctions and dense plaques occupied most of the cell border in all patients. Membrane caevolae occupied the spaces between these adherens junctions and dense plaques.

Conclusion: Immunohistochemistry and electron microscopy of the detrusor did not identify gap junctions. In organs such as the human uterus and mouse mammary glands, gap junctions have a rapid turnover with formation and involution occurring within several hours (2, 3). Many connexin subtypes have been identified. It could be argued that we failed to identify gap junctions in the overactive bladder because we happened to biopsy the bladders at a time when the junctions had undergone involution or the junctions were composed of connexin other than 26 and 43. In this study, the entire cell border stained positive to vinculin confirming that adherens junctions are the predominant and probably only junction present on detrusor smooth muscle cell membranes. Vinculin is a protein associated with adherens junctions and is likely to play an important role in the linkage of actin to the cell membrane. The function of adherens junctions is to mediate mechanical coupling between adjacent cell. Electron microscopy demonstrated the entire cell border to be occupied by adherens junctions, dense plaques (adherens 'hemijunctions') and caveolae leaving no space for gap junctions. We interpreted 'protrusion junctions' to be rudimentary adherens junctions rather than possible gap junctions as reported by Elbadawi et al (2). Connexin 43 was chosen because it has been found in the human uterus and was considered the most likely connexin to be identified if gap junctions were present in the human bladder. Connexin 26 has been identified in human cardiac muscle. The cause of increased membrane excitability in detrusor muscle in patients with bladder instability remains unanswered. This study failed to demonstrate that detrusor instability is caused by the presence of gap junctions.

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THE USE OF PERIPHERAL NEUROMODULATION FOR TREATMENT OF DETRUSOR OVERACTIVITY: AN URODYNAMIC BASED STUDY

Aim of Study: An urgency and frequency syndrome due to an overactive bladder can successfully be treated by afferent nerve stimulation of the S3 spinal regions. Aim of this study was to determine the efficacy of peripheral neuromodulation of the S3 region in patients with urgency-frequency syndrome due to an overactive bladder.
Patients and Methods: 15 patients (11 women and 4 men), suffering from urgency-frequency syndrome, as documented by a voiding chart were diagnosed with overactive bladder. Pelvic pain was assessed by an visual analogue scale (VAS). Full urodynamic work-up was performed before and after 12 peripheral stimulations with a 9V monopolar generator, the so-called Stoller Afferent Nerve Stimulator (SANS™) utilising a minimal invasive transcutaneous access to the posterior tibial nerves. Patients follow-up was for a mean (SD) 10.9 (4–15) months post treatment.
Results: No complications were observed. Reduction in pain was achieved in all patients, with a decrease in VAS from a mean (SD) of 7.6 (5–10) to 3.1 (1–7) (p=0.00049). Seven patients (46.7%) had a complete response and were considered